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Reflections on 50 Years of Newborn Screening

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Abstract

Newborn screening (NBS) began 50 years ago with the ability to screen for phenylketonuria from dried-blood spots and prevent long-term disability through dietary intervention. Now nearly all of the 4 million infants born in the United States are screened for a wide array of significant medical conditions by using dried-blood spots and point-of-care tests, leading to early diagnosis and treatment of more than 12 500 newborns each year.[1] NBS is an unqualified public health success; it saves lives, prevents severe disability, and is a good use of limited health care dollars. NBS is not a test, but a complex system that includes the initial screen to identify infants with a high probability of having the condition, a follow-up diagnostic test to identify true cases, and the ongoing treatment of the condition. To make this system efficient and effective requires several key players, including public health, primary and specialty care providers, and families. On this anniversary of NBS, we would like to share our reflections on these 3 perspectives, acknowledging that they capture only some of the important considerations and advances in NBS.

Keywords

newborn screening

THE PUBLIC HEALTH PERSPECTIVE: COLEEN BOYLE WRITES

Ten years ago, there was considerable variation in NBS, with as few as 3 to as many as 45 conditions included in state screening panels. In 2004, under guidance from the Health Resources Services Administration, the American College of Medical Genetics (ACMG), by using an expert-informed review process, recommended an NBS panel of 29 disorders.[2] Concurrent with this recommendation, the Newborn Screening Saves Lives Act authorized a federal advisory committee (the Advisory Committee on Heritable Disorders in Newborns

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and Children [ACHDNC]) to provide guidance to the Secretary of the Department of Health and Human Services on the practice of NBS in the United States. This led to the development of the ACHDNC Recommended Uniform Screening Panel (RUSP), which included as a baseline the ACMG 29 conditions. By 2009, most states were screening for the RUSP panel of disorders.[1]

Going forward, the ACHDNC has developed a transparent and evidence-based process for adding additional conditions to the RUSP using a balance of benefit, risk, and public health readiness for broad implementation, with the final decision resting with the Secretary of the Department of Health and Human Services.[3] Since its initiation, the congenital heart disease (CCHD), and a third, Pompe disease, awaiting a decision by the Secretary.

I expect that NBS will continue to expand beyond the traditional boundaries of a blood-spot–based program managed by the state public health departments. This raises the challenging questions about roles and responsibilities in universal screening. When screening for CCHD was considered by the ACHDNC, there was considerable debate on whether screening was really a surrogate for a standard of good clinical care, such as monitoring all newborns for hyperbilirubinemia, instead of a mandated component of an NBS program[4] In the case of CCHD, the ACHDNC determined that early detection and treatment were so clearly beneficial that the condition should be incorporated into the NBS system. However, because public health does not have a direct presence in birth hospitals, point-of-care NBS presents significant challenges in determining the optimal interface between public health and the hospitals, providers, and families. One of the important advantages of this partnership is the data-tracking and follow-up capacity of public health, providing key information that can serve as the linchpin for ongoing coordination between families and the clinical care systems.

THE HEALTH CARE PROVIDER PERSPECTIVE: JOSEPH BOCCHINI WRITES

Most of the attention in NBS is on the testing process, not the process of following up positive results and management after diagnosis. The initial challenge to busy health care providers is the timely follow-up of all screen-positive infants to identify the true-positives while being careful to explain to families that false-positives are not uncommon. The only way to do this well is to have a good understanding of the particular condition under consideration and what to do in the case of a screen-positive and true-positive result. Resources, such as the ACMG AC-Tion sheets, have been developed for the specific RUSP conditions.[5] Beyond diagnosis, the greatest challenge that I see is the ongoing management of the disorder. The benefit of NBS is from the presymptomatic initiation of treatment and continued follow-up over the life course of the child. We owe it to our patients to work to minimize barriers to comprehensive care (eg, facilitating equitable access to expensive therapies) and ensure that they receive good primary care (eg, immunizations).

There are many opportunities for pediatricians and other primary health care providers to participate and improve NBS. Examples include partnering with their state health departments to verify that all newborns are tested, working with families to make them

aware of results and what they mean long term, and helping to establish and maintain a medical home to support families in navigating the array of treatment options both at the outset and throughout childhood. Because many of these conditions are rare and evidence of effectiveness of treatment may be based on scant data, clinicians taking care of patients identified through NBS should partner with families, researchers, and public health agencies to collect the data necessary to improve treatments.[6] The exciting news is that because we have been screening for 50 years, we have several generations of NBS survivors who are charting the territory of living as an adult with an early childhood–onset condition. Targeted research is required to understand the longer-term consequences of 'treated' conditions, particularly the unanticipated consequences, such as maternal phenylketonuria.[7] Also, shifting the paradigm on what it means to live with these conditions will be required as we move forward, for affected individuals and their families and for their physicians and other health care providers.

THE FAMILY PERSPECTIVE: JAMES KELLY WRITES

At 4 months old, my only son, Hunter (February 14, 1997–August 5, 2005), was diagnosed with Krabbe leukodystrophy, a rare genetic disorder that affects the central and peripheral nervous systems. Although Hunter defied all medical expectations by living to be 8.5 years old, he still suffered greatly every day of his life.

After his diagnosis, my wife, Jill, and I formed the Hunter's Hope Foundation, named in his honor. While learning more about the only available treatment of Krabbe disease, a cord blood transplant, we also learned that for this treatment to be effective, it must be administered before the onset of symptoms, which in our son's case, was in his first few months of life. This is how our family and our foundation became involved in NBS, not only for Krabbe leukodystrophy, but for all diseases, for every child. Every time. Everywhere.

As a father, I am passionate about all children having the chance to dream, like I did, as a young boy who aspired to play football in the National Football League. Our children's chance to fulfill their own dreams should not depend on the state in which they are born. Any parent or family member whose child has been affected by NBS, or lack thereof, knows the importance of advocating for expanded NBS in every state, for every disease.

Since becoming involved in this vital public health program, NBS programs nationwide have come a long way, and, thankfully, 1 simple heel prick has saved thousands of children's lives. Family advocates are a big part of that success; they encourage lawmakers to adopt expanded NBS policies that ensure that no child has to needlessly suffer the way theirs has. They are a reminder, to the medical, legislative, and their own communities, that change must continue so future generations are protected, starting at birth.

It is inspiring to see firsthand the reward of our collective efforts. I can't tell you what a blessing it is to meet parents who introduce me to their son or daughter, saying, "If it weren't for NBS, my child wouldn't be here today." In fact, the first child diagnosed with and treated for Krabbe disease through New York's NBS program started kindergarten this past September.

Although there is still much work to be done, we are on a steadfast path for success. As we move forward, it is important for families to be actively engaged in discussions on gaps in the science so that NBS advancements and advocacy work as effectively as possible in improving children's health. Family and patient groups will continue to play a key role in facilitating the change that will affect our country's most precious and most vulnerable citizens: newborns.

THE NEXT 50 YEARS

Given the resounding success of NBS, increased attention will focus on improving understanding of the biochemical, genetic, or physiologic markers and effective interventions for other early childhood–onset conditions: the essential ingredients for universal screening. A key lesson from the past 50 years is the need to ensure that NBS continues to operate as a functioning partnership among public health, health care providers, and families. As NBS opportunities emerge, it is important that each of these partners remain actively engaged in evaluating readiness for universal screening to ensure that advances to detect a disorder complement our ability to effectively improve children's health.

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ABBREVIATIONS

ACHDNC	Advisory Committee on Heritable Disorders in Newborns and Children
ACMG	American College of Medical Genetics
CCHD	critical congenital heart disease
NBS	newborn screening
RUSP	Recommended Uniform Screening Panel

REFERENCES

1. Howell RR, Terry S, Tait VF, et al. Centers for Disease Control and Prevention (CDC). CDC Grand Rounds: Newborn screening and improved outcomes. MMWR Morb Mortal Wkly Rep. 2012; 61(21):390–393. [PubMed: 22647744]
2. Watson AS, Mann MY, Lloyd-Puryear MA, Rinaldo P, Howell RR. Newborn screening: toward a uniform screening panel and system. Genet Med. 2006; 8(suppl 1):1S–252S. [PubMed: 16783161]
3. Kemper AR, Green NS, Calonge N, et al. Decision-making process for conditions nominated to the Recommended Uniform Screening Panel: statement of the US Department of Health and Human Services Secretary's Advisory Committee on Heritable Disorders in Newborns and Children. Genet Med. 2014; 16(2):183–187. [PubMed: 23907646]

4. Kemper AR, Kus CA, Ostrander RJ, et al. United States Secretary of Health and Human Services Advisory Committee. A framework for key considerations regarding point-of-care screening of newborns. Genet Med. 2012; 14(12):951–954. [PubMed: 22899090]
5. ACMG. ACMG ACTSHEETS and Confirmatory Algorithms. Available at: https://www.acmg.net/ACMG/Resources/ACT_Sheets_and_Confirmatory_Algorithms/ACMG/Resources/ACT_Sheets_and_Confirmatory_Algorithms/ACT_sheets_Homepage.aspx?hkey51654e248-53f2-41a9-8d93-f3d96de05e0a.
6. Kemper AR, Boyle CA, Aceves J, et al. Long-term follow-up after diagnosis resulting from newborn screening: statement of the US Secretary of Health and Human Services' Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children. Genet Med. 2008; 10(4):259–261. [published correction appears in *Genet Med*. 2008; 10 (5):368]. [PubMed: 18414208]
7. Koch R. American Academy of Pediatrics, Committee on Genetics. Maternal phenylketonuria and tetrahydrobiopterin. Pediatrics. 2008; 122(6):1367–1368. [PubMed: 19047257]